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Silica gel-immobilised chiral 1,2-benzenedisulfonimide: a Brønsted acid heterogeneous catalyst for enantioselective multicomponent Passerini reaction†

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A chiral heterogeneous catalyst derivative of (−)-4,5-dimethyl-3,6-bis(1-naphthyl)-1,2-benzenedisulfonimide is proven here to be efficient in a three-component asymmetric Passerini protocol, carried out in a deep eutectic solvent. Reaction conditions are mild and green, while enantioselectivity is excellent. The catalyst was easily recovered and reused with no decrease in its catalytic activity.

Introduction

Organocatalysis has become a highly dynamic research area.[1] From the various groups of possible catalysts, Brønsted acids stand out as they present a range of benefits, including a lack of sensitivity to moisture and oxygen, ready availability, low cost and low toxicity.[2] The importance of catalysis also highlights the fact that the ninth principle (use of catalysts should be preferred wherever possible) of *Green Chemistry*[3] is devoted exclusively to this issue. In light of these, one of the key challenges for organic synthesis is to design and develop new and efficient catalysts that are active under mild and sustainably conditions.[4] In order to develop increasingly sustainable and eco-compatible procedures, a widespread practice in catalysis is to convert a successful homogeneous organocatalyst into an heterogeneous catalytic system.[5]

By using efficient heterogeneous catalysts, many processes can be carried out under milder conditions, significantly simplifying the usually cost-intensive and energy-consuming removal of the catalyst after reaction.[6] Moreover, such catalysts create the possibility of their effective and simple recycling. For these reasons, heterogeneous Brønsted acid organocatalysts can be used effectively as a toolbox for *Green Chemistry*.[7]

The preparation of enantiopure chemicals has been one of the most rapid growth areas in chemistry over the last decade with heterogeneous catalysis being recognised as providing new possibilities.[7] A plethora of different strategies has been developed to obtain enantioselectivity through heterogeneous catalysis: the use of chiral species to modify the solid surface,[8] homogeneous formation of a chiral complex before reaction at the solid surface[9] and the grafting of a chiral catalytic complex on a solid support, namely the heterogenised homogeneous catalyst.[10]

Our previous studies have seen 1,2-benzenedisulfonimide (**1**) and its chiral derivatives (−)-**2** and (−)-**3** used as excellent, versatile, safe and eco-friendly homogeneous Brønsted acid catalysts (Fig. 1).[11a–f]

More generally, chiral disulfonimides have received recently significant attention as robust and effective catalysts in asymmetric synthesis.[12] In fact, they are not only more acidic[11g] than phosphoric acids but they also have real C_2 symmetry which facilitates, especially in the presence of bulky substituents close to the acid site, an increase of stereochemical communication between the catalyst and the substrate.[12a] Furthermore, three chiral derivatives of disulfonimides namely adducts **4**, **5** and **6** (Fig. 2) are commercially available from Sigma-Aldrich.

In continuation of our research, we anchored, through an amide bond, an appropriately functionalised derivative of **1**, namely 1,2-benzenedisulfonimide-4-yl propionic acid (**8**), to a 3-

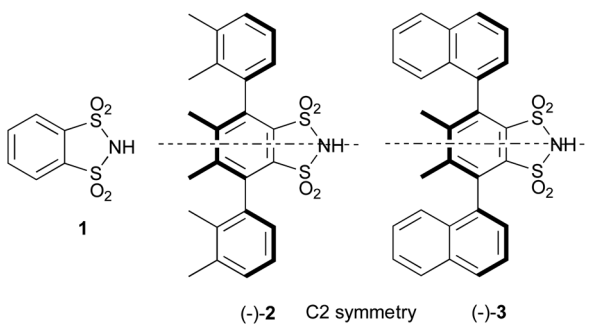

Fig. 1 1,2-Benzenedisulfonimide (**1**) and its chiral derivative (−)-**2** and (−)-**3**.

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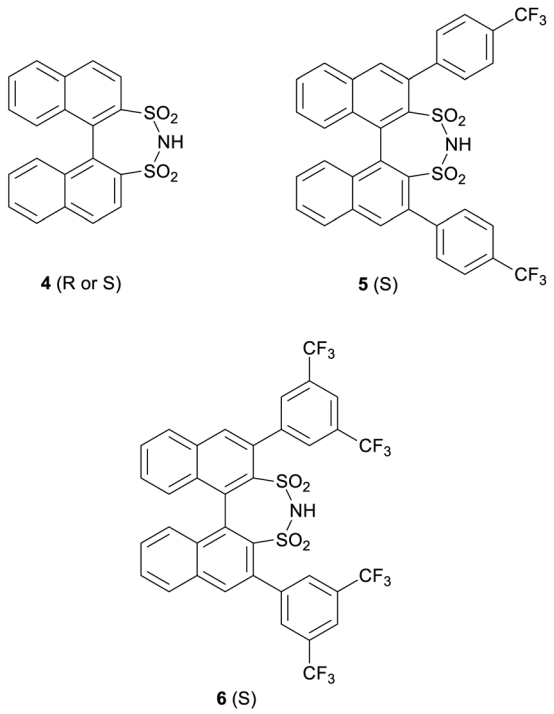


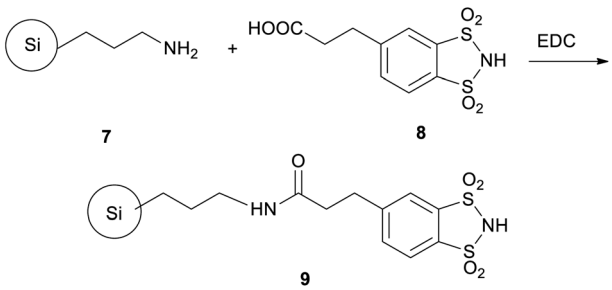
Fig. 2 Commercial disulfonimides.

aminopropyl functionalized silica gel support (**7**) thus obtaining a new specie having increased robustness and recyclability with respect to (**1**), furthermore paving the way for its successful employment in heterogeneous catalysis (**9**; Scheme 1).[13]

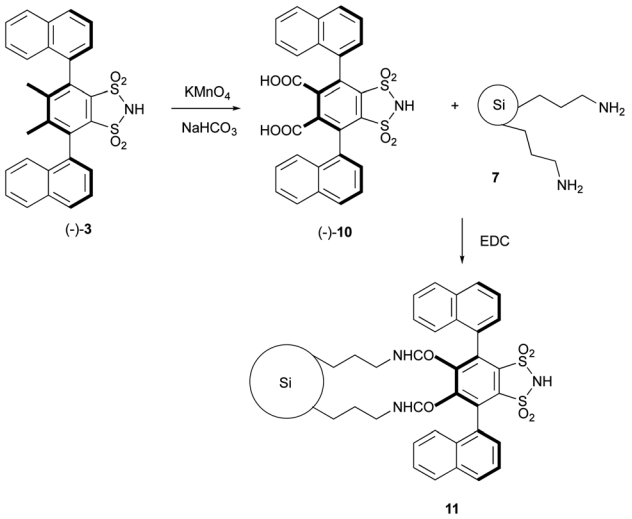
Result and discussion

Preparation of the catalyst 11

Encouraged by above results, in order to transform homogeneous chiral catalysts (−)-**3** into an efficient heterogeneous catalytic system, our first goal was to immobilize (−)-**3** by means a strong covalent bond, namely an amide bond, on 3-aminopropyl functionalized silica gel (**7**; 1 mmol g^{-1} NH_2 loading), selected as the solid support because of its commercial availability, chemical inertness and low toxicity. Moreover, it displays excellent chemical stability, high thermal and mechanical robustness. In order to form an amide bond, we needed to presence of two carboxyl groups on the central benzene ring. This objective was easily achieved by oxidising the methyl groups of (−) **3** with $KMnO_4$ in a basic environment (Scheme 2), obtaining in this way (−)-4,5-dicarboxy-3,6-bis(1-naphthyl)-1,2-benzenedisulfonimide (**10**). As reported in our previous paper,[13] the condensation between NH_2 and COOH groups was promoted by *N*-(3-dimethylaminopropyl)-*N*-ethylcarbodiimide hydrochloride (EDC; Scheme 2). The material obtained was isolated *via* filtration over Büchner funnel and was washed firstly with dilute hydrochloric acid in order to fully restore the acid function of the sulfonimide and then with acetone in order to remove any possible organic residue.



Scheme 1 Synthesis of heterogeneous catalyst **9**.



Scheme 2 Synthesis of chiral heterogeneous catalyst **11**.

The analysis of the IR spectrum of this solid, compared with that of **10** and with that of **7**, confirmed that the anchoring occurred with the formation of an amide bond (Fig. 3). In fact, In the IR spectrum of **11**, two bands were evident at 1633 and 1542 cm^{-1}. The band at 1633 cm^{-1} is due to the CO stretching

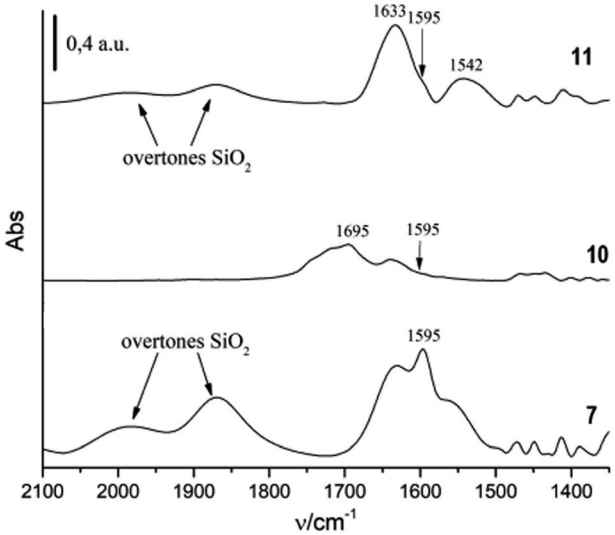


Fig. 3 IR spectra of **7**, **10** and **11**.

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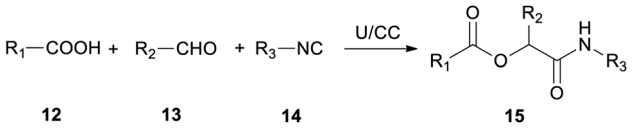

Scheme 3 Passerini reaction.

vibration, while the band at 1542 cm^{-1} is due to NH bending vibration of secondary amides. The weak band observed at 1595 cm^{-1} is probably associated to NH bending vibration of sulfonimide NH.

Once **11** was obtained, we decided to disfruit it as an heterogeneous chiral catalyst in order to develop a green asymmetric protocol for Passerini reaction (Scheme 3).[14]

Use of the catalyst 11 in asymmetric Passerini reactions

Multicomponent reactions (MCRs) are chemical transformations in which more than two reagents afford a new product which incorporates all of the atoms of the reagents, with an efficient one-step and high atom economy approach to building up complex molecules in compliance to the first principle of green chemistry.[15] In light of this, MCRs are a valid tool for achieving the goal of sustainable and eco-compatible chemistry. The Passerini reaction, first described about a century ago, is one of the oldest MCRs and it is the first isocyanide-based MCR.[14] It consists in one-pot, three component reaction of carboxylic acids **12** with aldehydes **13** (or ketones) and isocyanides **14**, offering an inexpensive and rapid way to generate a wide library of α-acyloxy carboxamides **15**. These compounds are present in the structures of many natural products, such as pharmacologically active depsipeptides and can lead to potentially bioactive peptidomimetics compounds.[16] As a stereocenter is formed, the development of enantioselective protocols has become a major goal. Although the literature highlights a number of examples of diastereoselective Passerini reactions[17] or asymmetric Passerini-like reactions,[18] only few examples are reported for asymmetric classic three-component passserini reactions.[19] These include, notably, a study by X.-Y. Liu, B. Tan *et al.*,[19d] involving the use of BINOL-based chiral phosphoric acids that efficiently catalyze the reaction, allowing for excellent enantiomeric excesses to be obtained. It must be stressed that this is the only example in which a homogeneous chiral Brønsted acid catalyst was applied in Passerini reactions. In light of this, an asymmetric and green version of classic Passerini reactions with a broad scope to application still remains a major goal to be achieved to date.

Optimization of the reaction conditions

Passerini reactions are usually carried out in common organic aprotic solvents.[14] However, in the last years, several optimizations have been implemented in order to minimise the ecological impact of this reaction, carrying out it in green solvents such ionic liquids,[20] water[21] or deep eutectic solvents (DESs).[22] DESs[23] are considered to be a non-toxic, environmentally benign, sustainable and easily accessible alternative to conventional organic solvents. They not only possess the advantages of ionic liquids, such as designability, chemical stability, and negligible vapour pressure, but they also provide many other advantages, such as tunability, low-cost and easily sourced raw materials, as well as green and simple synthesis without using other organic solvents. Therefore, DESs appear to be a good alternative to volatile organic solvents, and it can definitely be said that DESs have every chance of becoming "the reaction media of the century".[23b] In fact, since 2016,[24a] DESs have been profitably used as solvents for reactions carried out in

Table 1 Trial reactions

Entry	Solvent	Temp (°C)	Time (h)	Yield (%) of **15a**[a,b]
1	DCM	Rt	16	90
2	Toluene	Rt	18	85
3	THF	Rt	36	—[c]
4	DMSO	Rt	36	—[c]
5	EtOH	Rt	36	—[c]
6	H_2O	Rt	36	87
7	Neat	Rt	36	—[c]
8	Neat	60	16	45
9	Glycerol/choline chloride 4 : 1	Rt	26	—[c]
10	Glycerol/choline chloride 4 : 1	60	24	77
11	Urea/choline chloride 2 : 1	Rt	36	87
12	Urea/choline chloride 2 : 1	60	14	88

[a] Yields refer to pure and isolated **15a**. [b] The reaction was carried out with 1 mmol of **12a**, **13a** and **14a**. [c] After 36 h the reaction was not complete.

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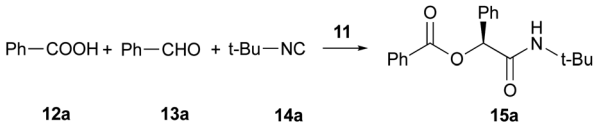
Table 2 Screening for solvents for chiral catalyst



Entry	Solvent	Temp (°C)	Time (h)	Yield (%) of **15a**[a,b]	ee[c] (%)
1	DCM	Rt	8	87	94.0
2	Toluene	Rt	10	90	94.2
3	H_2O	Rt	24	88	65.2
4	U/CC 2 : 1	Rt	20	87	94.8[d]
5	U/CC 2 : 1	60	12	90	22.3

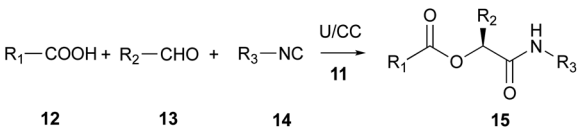
[a] Yields refer to pure and isolated **15a**. [b] The reaction was carried out with 1 mmol of **12a**, **13a**, **14a** and 5 mol% of catalyst **11**. [c] Ee was determined by chiral analyses on HPLC. [d] The same results were obtained using 10 mol% of catalyst **11**.

the presence of organic catalysts.[24b] However, despite these advantages, the employment of DESs in asymmetric organocatalyzed reactions remains very scarce[24c] but, given their promising features, it may be expected that many applications in these areas will appear in the coming years.

On this basis, a model reaction between benzoic acid (**12a**), benzaldehyde (**13a**), and *tert*-butyl isocyanide (**14a**) was studied (Table 1) at room temperature without any catalyst in several common organic solvents including DCM (Table 1; entry 1), toluene (Table 1; entry 2) THF (Table 1, entry 3), DMSO (Table 1; entry 4), EtOH (Table 1; entry 5) and in H_2O (Table 1; entry 6). It was not possible to carry out the reaction in neat conditions at room temperature (Table 1; entry 7). Furthermore, two different kinds of DESs were used, formed by a glycerol and choline chloride (GL/CC; ratio 4 : 1; Table 1, entries 9 and 10) and by urea and choline chloride (U/CC; 2 : 1 ratio; Table 1, entries 11 and 12) respectively. It is evident that U/CC DES is a good solvent for this reaction, providing yields of **15a** comparable to those obtained with toluene and DCM, though the reactions carried out in DCM or toluene are much faster than those carried out in DESs.

At the end of the reaction carried out in U/CC DES (Table 1; entry 11), after adding H_2O a white solid precipitated, which was separated by filtration and washed with small amounts of diethyl ether. In this way, pure **15a** was obtained without further purification. After this optimization, choosing U/CC DES as the privileged solvent, the scope of this reaction was extended using different carboxylic acids **12**, aldehydes **13** and isocyanides **14**. The results of these reactions are showed in a Table included in ESI† (Page 6). A number of aromatic **12a–d** or heteroaromatic carboxylic acids **12g** and aromatic aldehydes **13a–e** containing both electron-donating and electron-withdrawing groups were used and afforded excellent yields of **15**. Acids **12e–f** and aldehydes **13f–g** were also applied successfully in this reaction. Finally, it must be stressed that the reactions proceeded effectively with both aromatic **14b** and aliphatic isocyanides **14a**. On

Table 3 Scope of the Passerini reaction carried out in U/CC DES with chiral heterogeneous catalyst **11**



Entry	R_1 in RCOOH **12**	R_2 in RCHO **13**	R_3 in RNC **14**	Time (h)	**15**	Yield[a] (%)	Ee[b] (%)
1	Ph; **12a**	Ph; **13a**	*t*-Bu; **14a**	20	**15a**	87[c]	94.8
2	Ph; **12a**	3-$NO_2C_6H_4$; **13b**	*t*-Bu; **14a**	24	**15b**	93	96.4
3	Ph; **12a**	4-$MeOC_6H_4$; **13c**	*t*-Bu; **14a**	20	**15c**	85	96.8
4	Ph; **12a**	4-ClC_6H_4; **13d**	*t*-Bu; **14a**	22	**15d**	93	96.9
5	Ph; **12a**	4-MeC_6H_4; **13e**	*t*-Bu; **14a**	24	**15e**	87	97.6
6	Ph; **12a**	PhCH=CH; **13f**	*t*-Bu; **14a**	28	**15f**	86	92.7
7	Ph; **12a**	*i*-Pr; **13g**	*t*-Bu; **14a**	20	**15g**	87	95.5
8	4-$NO_2C_6H_4$; **12b**	Ph; **13a**	*t*-Bu; **14a**	24	**15h**	84	95.6
9	4-$MeOC_6H_4$; **12c**	Ph; **13a**	*t*-Bu; **14a**	30	**15i**	87	95.9
10	4-ClC_6H_4; **12d**	Ph; **13a**	*t*-Bu; **14a**	20	**15j**	90	96.8
11	Me; **12e**	Ph; **13a**	*t*-Bu; **14a**	20	**15k**	86	96.5
12	$PhCH_2$; **12f**	Ph; **13a**	*t*-Bu; **14a**	22	**15l**	87	93.1
13	3-Pyridyl; **12g**	4-ClC_6H_4; **13d**	*t*-Bu; **14a**	24	**15m**	78	96.5
14	Ph; **12a**	Ph; **13a**	2-Naphthyl; **14b**	20	**15n**	87	98.4
15	Ph; **12a**	4-ClC_6H_4; **13d**	2-Naphthyl; **14b**	20	**15o**	83	95.3
16	Me; **12e**	3-$NO_2C_6H_4$; 13b	2-Naphthyl; **14b**	24	**15p**	84	97.6
17	Me; **12e**	*i*-Pr; **13g**	2-Naphthyl; **14b**	22	**15q**	86	96.1

[a] Yields refer to pure and isolated **15**. Times and yields refer to the reactions carried out with 1 mmol of **12a**, **13a**, **14a** with chiral catalyst **11** (5% mol). [b] Enantiomeric excess was determined by chiral analyses on HPLC (ee). [c] The same results were obtained using 10 mol% of catalyst **11**.

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Table 4 Recovery and reuse of catalyst **11**

Entry	Time (h)	Yield (%) of **15a**[a,b]	Recovery of **11**	ee (%) in **15a**
1	24	87	0.06 g[c]	94.8
2	24	85	0.06 g[d]	95.0
3	24	87	0.06 g[e]	93.2
4	28	88	0.05 g[f]	93.1
5	28	84	0.05 g	94.0

[a] Yields refer to the pure and isolated product. [b] The reaction was performed at room temperature with 1 mmol of **12a**, **13a**, **14a** and 5 mol% of **11**. [c] Recovered **11** was used as a catalyst in entry 2. [d] Recovered **11** was used as a catalyst in entry 3. [e] Recovered **11** was used as a catalyst in entry 4. [f] Recovered **11** was used as a catalyst in entry 5.

the contrary, the reaction of acetophenone (**13h**) could not reach completion.

Whit these optimized conditions in hand, we chose four kinds of solvents, namely DCM, toluene, H_2O and DES urea/choline chloride and we carried out the reactions in the presence of heterogeneous chiral catalysts **11**. We successfully gained good enantiomeric excesses in the reaction carried out with both DCM or toluene (Table 2; entries 1 and 2) and U/CC DES (Table 2; entry 4) at room temperature. It is interesting to note that the reaction times are significantly lower than the reactions carried out in the absence of a catalyst.

Then, using U/CC at room temperature as favorite and green solvent, we expanded the reaction to the same terms previously used, obtaining approximately the same yields as the reactions carried out in the absence of catalyst and excellent enantiomeric excesses, always higher than 92% (Table 3). The heterogeneous catalyst **11** was almost completely recovered by easy filtration on a Büchner funnel and reused four consecutive runs. The results are listed in Table 4, where it can be seen that the yields of **15a** and the enantioselectivity were consistently good over the various runs.

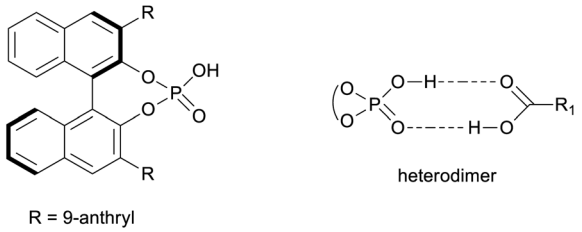
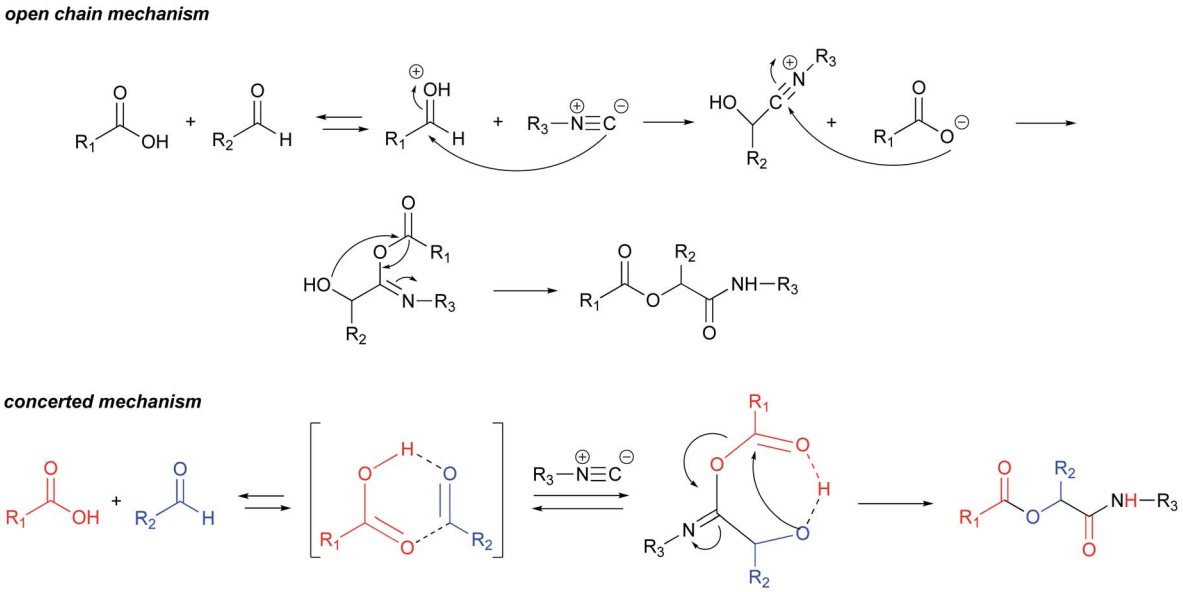


Fig. 4 Key intermediates for chiral phosphoric acid catalysed Passerini reaction.

Furthermore, also the solvent system U/CC was easily recovered at the end of the reactions (for details see Experimental) and was used in three consecutive runs, without observing a decrease in the yield of **15a** and in the enantioselectivity of the reaction.

Mechanism of the reaction

Although Passerini's reaction has been known for nearly a century, some uncertainties remain regarding its exact mechanism.[25] It has been hypothesized that the reaction can proceed either *via* an "open chain" mechanism (where the key intermediates is a nitrilium ion) or *via* a "concerted mechanism" (where an intermediate nitrilium ion is not formed; Scheme 4). In polar solvents such as methanol or water, the reaction should proceed with an "open chain mechanism"[26] *via* protonation of the carbonyl component followed by nucleophilic addition of the isocyanide and carboxylate residue, respectively. The resultant intermediate undergoes acyl group transfer to give the α-acyloxyamide. In nonpolar solvents, a "concerted mechanism" should be favored: a trimolecular reaction between the isocyanide, the carboxylic acid, and the carbonyl in a sequence



Scheme 4 Proposed mechanisms for Passerini reaction.

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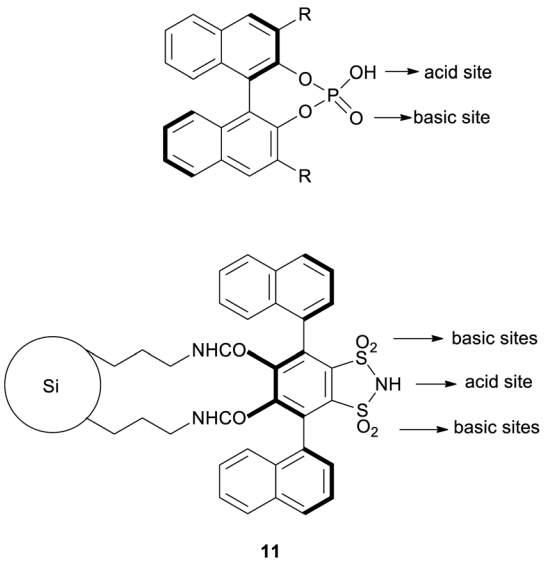


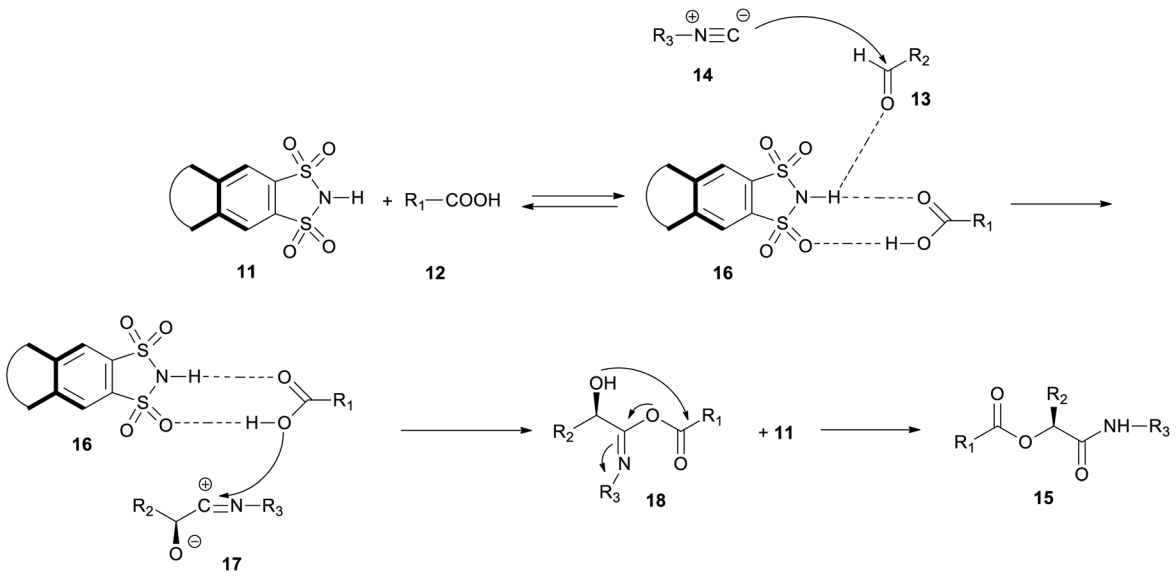
Fig. 5 Disulfonimide **11** as multidentate system.

of nucleophilic additions has been proposed, without the formation of a real nitrilium intermediate. The transition state is depicted as a 5-membered ring. The last step (Mumm rearrangement) includes the acyl migration to the neighbouring hydroxyl group to produce the desired ester.

In the already mentioned elegant paper by Liu and Tan,[15d] an efficient enantioselective Passerini reaction was developed in the presence of a chiral phosphoric acid catalyst, deriving from BINOL. The authors proposed an interesting mechanism in which, inspired by List's previous studies,[27] a key intermediate, such as heterodimer, could form between the chiral phosphoric acid catalyst and carboxylic acid, creating a chiral environment suitable for asymmetric induction of the reaction (Fig. 4).

Regarding the Passerini reactions carried out in the presence of **11**, we believe that two possible mechanisms can be hypothesized. In the first and, in particular, in the reactions carried out with DCM and toluene (apolar or not very polar solvents), heterogeneous catalyst **11** could act similarly to phosphoric acid. In fact, if the structure of sulfonimides is compared with that of the phosphoric acids, it is clear that both have acidic and basic sites. Indeed, if the phosphoric acid can be considered a bidentate system, sulfonimides, thanks to the presence of the SO_2 group, can be considered a multidentate system that can form five hydrogen bonds (Fig. 5).[28]

Moreover, the high acidity of catalyst **11** (higher than that of a phosphoric acid) could, on the one hand, facilitate the formation of the heterodimer and, on the other hand, make the carboxylic acid more nucleophilic, and therefore more reactive. Indeed, the reaction times carried out in the presence of **11** (8 h. Table 3; entry 1) were significantly lower than those carried out without **11** (16 h. Table 1; entry 1). Therefore, thanks to the formation of the heterodimer **16** and its interaction with aldehyde **13**, a chiral fashion is created, facilitating the enantioselective attack of the nucleophile isocyanate **14**, with the formation of a nitrilium intermediate **17**. It then undergoes nucleophilic attack by the acid **12**; finally, Mumm rearrangement of the imidate **18** leads to the formation of the final product **15** (Scheme 5). In a recent review of Passerini reaction mechanism, Morokuma demonstrated, using DFT calculations, that the nitrilium intermediate is stable in solution and the rate of the reactions is significantly higher in low-polar solvents (*e.g.* DCM) not because the nitrilium ion is not formed, as is commonly believed, but because a network of hydrogen bonds makes its formation more difficult.[24] This could be confirmed by our experimental data: the reactions carried out in DCM (8 h. Table 3; entry 1) are much faster than the reactions carried out in DES (20 h. Table 2; entry 1). In his mechanism hypothesis, Morokuma believes that the Mumm rearrangement can be catalyzed by a second carboxylic acid



Scheme 5 Proposed mechanism of Passerini reaction in DCM catalysed by **11**.

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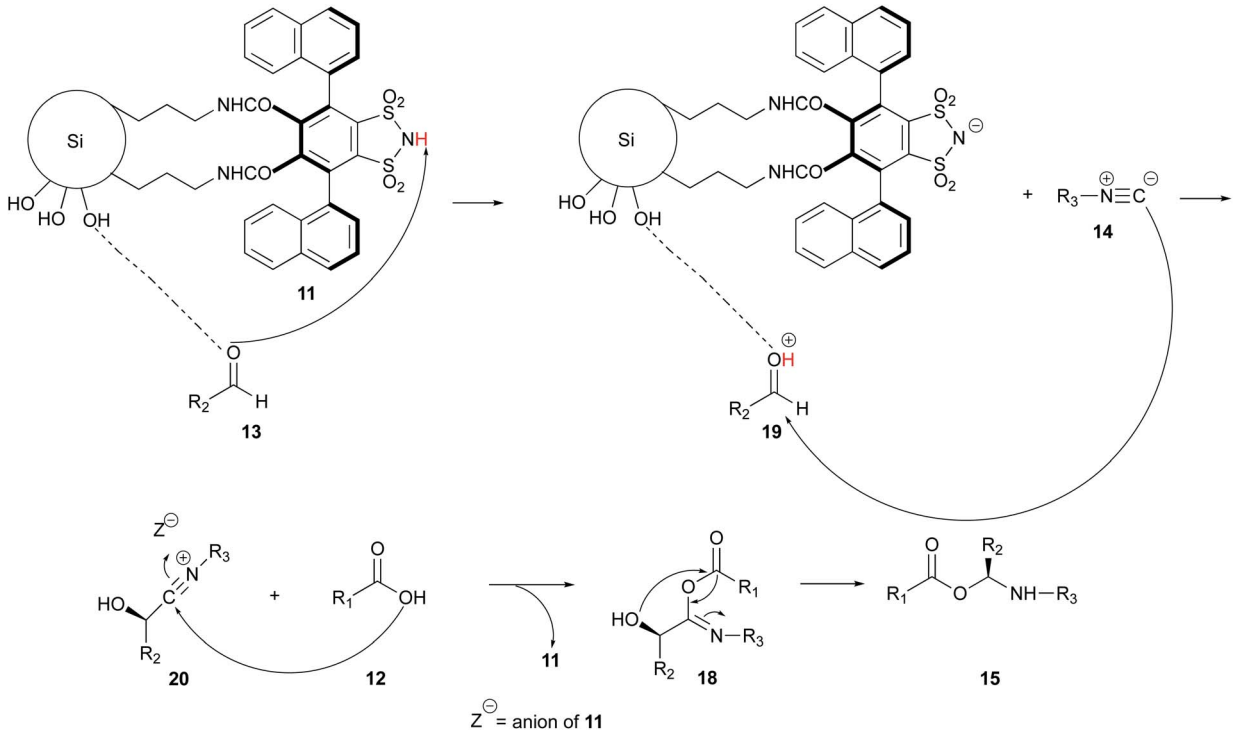

Scheme 6 Proposed mechanism of Passerini reaction in DES catalysed by **11**.

molecule. Therefore, it might be is possible that the acid catalyst also plays a role in facilitating Mumm rearrangement.

On the other hand, it is dubious that the reaction occurs the same way in DES. The polarity of U/CC DES,[29] far superior to that of DCM or toluene, should favour an "open chain" mechanism. Therefore, we assume that, in DES, the reaction could occur precisely with this mechanism (Scheme 6). We think that the activation of aldehyde is due to the action of **11**, mainly by means of the acid site of the sulfonimide (NH group), but also with those belonging to the silica support. The weak basicity of U/CC DES[30] should not hinder this activation After its formation, **19** undergoes the enantioselective attack of **14** with the formation of the intermediate **20** which, in turn, undergoes the nucleophilic attack of the OH of **12**. The intermediate **18** is obtained and finally the latter, by means of Mumm rearrangement, gives the product **15**. Assuming the above mechanism, this reaction may therefore be counted as an asymmetric counteranion-directed catalysis (ACDC), according to list classification.[31]

Conclusions

In this paper, a sustainable version of asymmetric three component Passerini reaction has been proposed. In our conditions, we are able to achieve important green benefits, including the use of a DES as a solvent at room temperature, the use of a novel and safe heterogeneous catalyst, its complete recovery and reuse, stoichiometric reagent ratio and mild reaction conditions. High yields of target products (17 examples) and excellent enantiomeric excess (17 examples; average 96%) have been obtained; furthermore, they are obtained in adequate purity, making further chromatographic purification unnecessary. It must be stressed that the use of chiral disulfonimides as acid catalysts in asymmetric synthesis, thanks to the important advantages they provide, is now widely consolidated. However, the synthetic protocols for obtaining such catalysts can be quite complex; this is proven by the fact that the cost of the commercially available disulfonimides is very high. Therefore, a disulfonimide which acts as a heterogeneous catalyst and which can be used several times without losing its catalytic activity, certainly represents an added value for this family of catalysts.

Experimental

General remarks

Analytical grade reagents were used and reactions were monitored by GC, GC-MS. Column chromatography were performed on Merck silica gel 60 (70–230 mesh ASTM) and GF 254, respectively. Petroleum ether (PE) refers to the fraction boiling in the range 40–70 °C. Mass spectra were recorded on an HP 5989B mass selective detector connected to an HP 5890 GC with a cross-linked methyl silicone capillary column. HRMS analyses were performed on an Orbitrap Fusion instrument. HPLC analyses were performed on HPLC Waters 1525 connected to a column Chiralpack IG-SFC. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Jeol ECZR spectrometer at 600 and 150 MHz respectively. IR spectra were recorded on a IR PerkinElmer UATR-two spectrometer. Alternatively, IR spectra of **7**, **10** and **11** were recorded in the form of self-supporting pellets (using the powders either as such or in KBr dispersion) by means of a Bruker IFS Vector 22 spectrophotometer (resolution 4 cm^{-1}), equipped with a MCT cryodetector. For the determination of

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optical rotations, a Jasco P-2000 polarimeter was used. (−)-4,5-Dimethyl-3,6-bis(1-naphthyl)-1,2-benzenedisulfonimide (**3**) was synthesized as previously reported by us.[11d] Urea/choline chloride DES were prepared as reported in the literature.[32] All reagents were purchased from Sigma-Aldrich or Alfa-Aesar. Structures and purity of all the products obtained in this research were confirmed by their spectral (NMR, MS, IR) data. Yields and enantiomeric excesses of the pure (GC, GC-MS and NMR) and isolated **15** are reported in Table 2. Satisfactory microanalyses were obtained for new compounds.

Synthesis of (−)-4,5-dicarboxy-3,6-bis(1-naphthyl)-1,2-benzenedisulfonimide 10

To a solution of (−)-4,5-Dimethyl-3,6-bis(1-naphthyl)-1,2-benzenedisulfonimide (**3**, 1 mmol, 0.50 g) in H_2O (15 mL) were added $KMnO_4$ (26 mmol, 4.11 g) and Na_2CO_3 (18 mmol, 1.91 g). The resulting mixture was heated at 100 °C for 24 h. In order to remove $KMnO_4$, the mixture was filtered on a Büchner funnel and the purple filtrate was decoloured with charcoal. H_2O was evaporated under reduced pressure. The crude residue, dissolved in H_2O was passed through a Dowex (HCR-W2) column (H_2O), affording pure **10** (0.56 g, 100% yield) as a grey waxy solid.

$[\alpha]_D^{22}$-25.6 (c 0.15 in CH_2Cl_2). Found: C, 60.48; H, 3.41; N 2.38. Calc. for $C_{28}H_{17}NO_8S_2$: C, 60.10; H, 3.06; N, 2.50. ν_{max}/cm^{-1} 3012 (OH), 1695 (CO). δ_H (600 MHz, D_2O) 7.85–7.49 (m, 6H), 7.47–7.34 (m, 8H). δ_C (150 MHz, D_2O) 167.9, 136.2, 133.7, 133.5, 132.0, 129.6, 128.5, 128.3, 127.8, 127.8, 126.4, 126.2, 125.9. HRMS (ESI, *m*/*z*): 560.05 (M + H$^+$).

4,5-Dicarboxy-3,6-bis(1-naphthyl)-1,2-benzenedisulfonimide immobilized on 3-aminopropyl functionalized silica gel (11)

Adduct **10** (0.5 mmol, 0.28 g) and *N*-(3-dimethylaminopropyl)-*N*-ethylcarbodiimmide hydrochloride (EDC, 1.5 mmol, 0.28 g) were added to a stirred suspension of 3-aminopropyl functionalized silica gel **7** (1 g; 1 mmol g^{-1} NH_2) in H_2O (5 mL). The reaction mixture was vigorously stirred at r.t. for 5 h. The resulting white solid was filtered over Büchner funnel. Firstly was washed with 10 mL of 2 N HCl (in order to fully restore the sulfonimide acidity) and then with 10 mL of acetone (in order to remove eventual organic residues arising from **11** and catalyst); lastly, it was dried in oven at 70 °C overnight. After this treatment, 1.10 g of **11** was obtained (87% yield). Aqueous and acetone washings were collected and evaporated under reduced pressure. No traces of possible unreacted **10** were detected. In a collateral proof 2 (1 g) and **10** (0.5 mmol, 0.28 g) were reacted without EDC. IR spectrum of the obtained solid (0.99 g), included in ESI.† (Page 5), was markely different from that of **11** and the characteristic bands of the amide bond were not present.

11 as a heterogeneous catalyst in Passerini reactions. General procedure

Chiral heterogeneous catalyst **11** (1; 5 mol%, 0.06 g equivalent to 0.05 mmol of immobilized acid) was added at room temperature to a stirring mixture of aldehyde **13** (1 mmol) and carboxylic acid **12** (1 mmol) in urea/choline chloride (U/CC) deep eutectic solvent system (5 mL). After 10 min, isocyanide **14** (1 mmol) was added. The mixtures were stirred at room temperature for the times listed in Table 3 (yield in bracket and in blue), until the GC and GC-MS analyses showed the complete disappearance of starting compounds and the complete formation of α-acyloxyamide **15**. In order to recover the catalyst, the reaction mixture was filtered on a Hirsch funnel and recovered solid was washed with of H_2O. Recovered catalyst was dried in oven at 70 °C. After this treatment the recovered catalyst (0.06 g, 100% of recovery) was reused in other four consecutive catalytic runs as reported in Table 4. The yield and the enantiomeric excess of **15a** and the recovery of **11** were always consistently good. Cold H_2O (5 mL) was added to the filtrate, under vigorous stirring. A white solid formed and was recovered by filtration on a Hirsch funnel. It was washed with additional cold H_2O and diethyl ether (2 mL each). Virtually pure (GC, GC-MS, ^{1}H NMR, ^{13}C NMR) **15** was obtained. The liquid residue was collected and, in order to remove H_2O and diethyl ether, was evaporated under reduced pressure. The recovered U/CC solvent system showed NMR and IR spectra almost identical to the initial one (ESI†). Physical and spectral data of adducts **15** are reported in ESI.† After the above work-up, enantiomeric excesses were measured. However, in order to verify the accuracy of these measures, the crude residue of **15a**, obtained after extraction with DCM, was chromatographed on a short column (eluent: EP–EtOEt, 4 : 1) and then enantiomeric excess was determined. The values were identical (96.4% on HPLC).

Author contributions

AA was responsible of the chiral analyses; FM took care of the synthesis of the heterogeneous chiral catalyst. SD coordinated the research. From the experimental point of view he performed the Passerini reactions with the chiral catalyst and he took care of the writing of the paper.

Conflicts of interest

There are no conflicts to declare.

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